

CLAIMS

What we claim is:

1. A recombinant conjugate antibody molecule, comprising a monoclonal antibody moiety specific for a surface structure of antigen presenting cells genetically modified to contain at least one antigen moiety exclusively at at least one preselected site on said monoclonal antibody moiety, whereby said conjugate antibody molecule is capable of delivering said antigen moiety to the antigen presenting cells of a host and capable of eliciting an immune response to said antigen moiety in the host.

2. The molecule of claim 1 wherein said antigen presenting cells are selected from the group consisting of class I major histocompatibility expressing cells, class II major histocompatibility expressing cells, dendritic cells and CD4⁺ cells.

3. The molecule of claim 1 wherein said at least one antigen moiety is located at at least one end of at least one of the heavy and light chains of said monoclonal antibody moiety.

4. The molecule of claim 3 wherein said at least one antigen moiety is located at the C-terminal end of said at least one of the heavy and light chains of said monoclonal antibody moiety.

5. The molecule of claim 4 wherein said at least one antigen moiety is located at the C-terminal end of both said heavy and light chains of said monoclonal antibody moiety.

6. The molecule of claim 5 wherein said at least one antigen moiety is directly linked to the C-terminal end of both said heavy and light chains of said monoclonal antibody moiety.

7. The molecule of claim 6 wherein said at least one antigen moiety is an inherently weakly-immunogenic antigen moiety.

SEARCHED INDEXED
SERIALIZED FILED

SEARCHED
INDEXED
SERIALIZED
FILED
JUN 14 1994

8. The molecule of claim 6 wherein said at least one antigen moiety comprises a plurality of antigen moieties.

9. The molecule of claim 8 wherein said plurality of antigen moieties is a plurality of a single antigen moiety.

10. The molecule of claim 8 wherein said plurality of antigen moieties is a plurality of different antigenic moieties.

11. The molecule of claim 7 wherein said at least one antigen moiety is a peptide having from 6 to 100 amino acids and containing at least one epitope.

12. A nucleic acid molecule, comprising a first nucleotide sequence encoding a chain of a monoclonal antibody specific for a surface structure of antigen-presenting cells selected from the group consisting of the heavy chain and the light chain of the monoclonal antibody, a second nucleotide sequence encoding at least one antigen and a third nucleotide sequence comprising a promoter for eukaryotic cell expression of a fusion protein comprising said monoclonal antibody chain and said at least one antigen.

13. The nucleic acid molecule of claim 12 wherein said encoded chain is the heavy chain of the monoclonal antibody.

14. The nucleic acid molecule of claim 12 wherein said encoded chain is the light chain of the monoclonal antibody.

15. The nucleic acid molecule of claim 12 wherein antigen presenting cells are selected from the group consisting of class I major histocompatibility expressing cells, class II major histocompatibility expressing cells, dendritic cells and CD4⁺ cells.

16. The nucleic acid molecule of claim 12 wherein said first nucleotide sequence and said second nucleotide sequence are directly linked in a single transcriptional unit under control of said promoter.



17. The nucleic acid molecule of claim 16 wherein said third nucleotide sequence is disposed at the 5' end of said first nucleotide sequence.

18. A vector comprising the nucleic acid molecule of claim 12, comprising a first nucleic acid sequence.

19. The vector of claim 18 containing a first nucleic acid molecule comprising a first nucleotide sequence encoding the heavy chain of a monoclonal antibody specific for a surface structure of antigen-presenting cells, a second nucleotide sequence encoding at least one antigen and a third nucleotide sequence comprising a promoter for eukaryotic cell expression of a fusion protein comprising said monoclonal antibody heavy chain and said at least one antigen as a first transcriptional unit, and a second nucleic acid molecule comprising a first nucleotide sequence encoding the light chain of a monoclonal antibody specific for a surface structure of antigen-presenting cells, a second nucleotide sequence encoding at least one antigen and a third nucleotide sequence comprising a promoter for eukaryotic cell expression of a fusion protein comprising said monoclonal antibody light chain and said at least one antigen as a second transcriptional unit.

20. The vector of claim 19 having the characteristic properties of plasmid pCMVdhfr.chLCHC.

21. A method of making a conjugate antibody molecule comprising a monoclonal antibody moiety specific for a surface structure of antigen-presenting cells and at least one antigen moiety, which comprises:

constructing a first nucleic acid molecule containing a first nucleotide sequence encoding a heavy chain of said monoclonal antibody and a second nucleotide sequence encoding at least one antigen,

constructing a second nucleotide acid molecule containing a first nucleotide sequence encoding a light chain of said monoclonal antibody and a second nucleotide

sequence encoding said at least one antigen, and coexpressing said first and second nucleic acid molecules in mammalian cells to form said conjugate antibody molecule.

22. The method of claim 21 wherein said coexpression of said first and second nucleic acid molecules includes constructing an expression vector containing said first and second nucleic acid molecules as independent transcriptional units.

23. The method of claim 22 wherein each said independent transcriptional unit includes a promoter operable in mammalian cells to direct said coexpression.

24. The method of claim 23 wherein said expression vector has the characteristic properties of plasmid pCMVdhfr.chLCHC.

25. The method of claim 23 wherein said coexpression includes secretion of said conjugate antibody molecule and further separating and purifying said conjugate antibody molecule.

26. The method of claim 25 wherein said purification comprises binding of the conjugate antibody molecule to protein A and selective elution of said conjugate antibody molecule from protein A.

27. An immunogenic composition, comprising a conjugate antibody molecule comprising a monoclonal antibody moiety specific for a surface structure of antigen presenting cells genetically modified to contain at least one antigen moiety exclusively at at least one preselected site on said monoclonal antibody moiety, whereby said conjugate antibody molecule is capable of delivering said antigen moiety to the antigen presenting cells of a host and capable of eliciting an immune response to said antigen moiety in the host or a nucleic acid molecule comprising a first nucleotide sequence encoding a chain of a monoclonal antibody specific for a surface structure of antigen-presenting cells selected from the group

May

John M. Clark
consisting of the heavy chain and the light chain of the monoclonal antibody, a second nucleotide sequence encoding at least one antigen and a third nucleotide sequence comprising a promoter for eukaryotic cell expression of a fusion protein comprising said monoclonal antibody chain and said at least one antigen.

28. The immunogenic composition of claim 27 formulated as a vaccine for in vivo administration to a host to confer protection against disease caused by a pathogen producing said at least one antigen.

29. A method of generating an immune response in a host, comprising administering thereto an immuno-effective amount of an immunogenic composition comprising a conjugate antibody molecule comprising a monoclonal antibody moiety specific for a surface structure of antigen presenting cells genetically modified to contain at least one antigen moiety exclusively at at least one preselected site on said monoclonal antibody moiety, whereby said conjugate antibody molecule is capable of delivering said antigen moiety to the antigen presenting cells of a host and capable of eliciting an immune response to said antigen moiety in the host or a nucleic acid molecule comprising a first nucleotide sequence encoding a chain of a monoclonal antibody specific for a surface structure of antigen-presenting cells selected from the group consisting of the heavy chain and the light chain of the monoclonal antibody, a second nucleotide sequence encoding at least one antigen and a third nucleotide sequence comprising a promoter for eukaryotic cell expression of a fusion protein comprising said monoclonal antibody chain and said at least one antigen.

30. A method of determining the presence of a selected antigen in a sample, which comprises:

(a) immunizing a host with a conjugate antibody molecule, comprising a monoclonal antibody moiety

specific for a surface structure of antigen presenting cells genetically modified to contain at least one antigen moiety exclusively at at least one preselected site on said monoclonal antibody moiety, whereby said conjugate antibody molecule is capable of delivering said antigen moiety to the antigen presenting cells of a host and capable of eliciting an immune response to said antigen moiety in the host, wherein said at least one antigen moiety is said selected antigen to produce antibodies specific to said selected antigen;

(b) isolating said antibodies;

(c) contacting the sample with the isolated antibodies to produce complexes comprising any selected antigen in the sample and said selected antigen-specific antibodies; and

(d) determining production of the complexes.

31. A diagnostic kit for determining the presence of a selected antigen in a sample, comprising:

(a) a conjugate antibody molecule comprising a monoclonal antibody moiety specific for a surface structure of antigen presenting cells genetically modified to contain at least one antigen moiety exclusively at at least one preselected site on said monoclonal antibody moiety, whereby said conjugate antibody molecule is capable of delivering said antigen moiety to the antigen presenting cells of a host and capable of eliciting an immune response to said antigen moiety in the host, wherein the at least one antigen moiety is said selected antigen;

(b) means for detecting the production of complexes comprising any selected antigen in the sample and selected antigen-specific antibodies to said selected antigen; and

antigen; and
(c) means for determining production of the
complexes.

32. A method for producing antibodies specific for a

selected antigen comprising:

(a) immunizing a host with an effective amount of an immunogenic composition comprising a conjugate antibody molecule comprising a monoclonal antibody moiety specific for a surface structure of antigen presenting cells genetically modified to contain at least one antigen moiety exclusively at at least one preselected site on said monoclonal antibody moiety, whereby said conjugate antibody molecule is capable of delivering said antigen moiety to the antigen presenting cells of a host and capable of eliciting an immune response to said antigen moiety in the host or a nucleic acid molecule comprising a first nucleotide sequence encoding a chain of a monoclonal antibody specific for a surface structure of antigen-presenting cells selected from the group consisting of the heavy chain and the light chain of the monoclonal antibody, a second nucleotide sequence encoding at least one antigen and a third nucleotide sequence comprising a promoter for eukaryotic cell expression of a fusion protein comprising said monoclonal antibody chain and said at least one antigen, wherein said at least one antigen is the selected antigen to produce antibodies specific for the selected antigen; and

(b) isolating the antibodies from the host.

33. A method of producing monoclonal antibodies specific for a selected antigen comprising:

(a) administering an immunogenic composition comprising a conjugate molecule comprising a monoclonal antibody moiety specific for a surface structure of antigen presenting cells genetically modified to contain at least one antigen moiety exclusively at at least one preselected site on said monoclonal antibody moiety, whereby said conjugate antibody molecule is capable of delivering said antigen moiety to the antigen presenting cells of a host and capable of eliciting an immune response to

884770-16020060

said antigen moiety in the host, or a nucleic acid molecule comprising a first nucleotide sequence encoding a chain of a monoclonal antibody specific for a surface structure of antigen-presenting cells selected from the group consisting of the heavy chain and the light chain of the monoclonal antibody, a second nucleotide sequence encoding at least one antigen and a third nucleotide sequence comprising a promoter for eukaryotic cell expression of a fusion protein comprising said monoclonal antibody chain and said at least one antigen, wherein said at least one antigen is the selected antigen to at least one mouse to produce at least one immunized mouse;

- (b) removing B-lymphocytes from the at least one immunized mouse;
- (c) fusing the B-lymphocytes from the at least one immunized mouse with myeloma cells, thereby producing hybridomas;
- (d) cloning the hybridomas;
- (e) selecting clones which produce anti-selected antigen antibody;
- (f) culturing the anti-selected antigen antibody-producing clones; and then
- (g) isolating anti-selected antigen antibodies from the cultures.